ETHICAL DILEMMA'S OF VENOUS THROMBO-EMBOLISM IN FINANCIAL RESOURCE STARVED ENVIRONMENT

Taole Mokoena DPhil FRCS Department of Surgery University of Pretoria





The Magnitude of Venous Thrombo-Embolism

- Hospitalization is a major risk for in-hospital DVT and pulmonary embolism
- Some surgical diseases and procedures *per se* are added risk factors
- Pulmonary embolism is dreaded cause of major morbidity and mortality in hospitalised patients

Patient information	DVT prevalence %
Internal medicine	10 - 20
General surgery	15 - 40
Major gynaecological surgery	15 - 40
Major urological surgery	15 - 40
Neurosurgery	15 - 40
Stroke	15 - 40
Hip and knee replacement surgery	40 - 60
Hip fractures	40 - 60
Polytrauma	40 - 80
Spinal cord injury	60 - 80
Critical care	10 - 80

Table 1. DVT prevalence in various patient populations

Jacobson BF SAMJ 2013

	Surgical patients	Medical patients
Low VTE risk	 Surgery lasting <30 minutes Injuries without or with only minor soft-tissue trauma No or only minor additional predisposing risk factors 	 Infection or acute inflammatory diseases without bed rest Central venous catheters No or only minor additional predisposing risk factors
Moderate VTE risk	 Surgical procedures of longer duration Immobilisation of lower limb with plaster cast Lower limb arthroscopic procedures. No or only minor additional predisposing risk factors 	 Acute cardiac insufficiency (NYHA III/IV) Acute decompensated COPD without ventilation Infection or acute inflammatory diseases with bed rest Malignant disease No or only minor additional predisposing risk factors
High VTE risk	 Major surgical procedures for malignancy Multiple trauma or severe trauma of the spine, vertebra or lower limbs Major orthopaedic surgery, e.g. hip or knee replacement Major surgical procedure of cardiothoracic and pelvic region 	 Stroke with paralysis Acute decompensated COPD with ventilation Sepsis ICU patients

Jacobson BF SAMJ 2013

Prophylaxis Against Venous Thrombo-Embolic Phenomena

Medical Anticoagulant Prophylaxis Oral

- Anti-vitamin K viz Coumarins e.g. Warfarin
- Anti-factor Xa e.g. Rivaroxaban (Xarelto)

Parenteral

- Heparin
- Low molecular Heparin eg. Enoxaparin (Clexane)

Passive Mechanical Prophylaxis

- Graduated elastic stockings
- Intermittent pneumatic compression devices
- Foot compression and passive movement devices

Intravenous IVC Filter Prophylaxis

Diagnosis of DVT and PE

- D-dimer measurement not reliable after surgery
- Venography is gold standard but invasive
- Venous Doppler
- VQ scan
- CT angiography
- MRI angiography (not practical in ICU pts)

Treatment of DVT and PE

- Therapeutic doses of anticoagulants against propagation
- Thrombolytic treatment
 - tPA / urokinase
 - Streptokinase
- Thrombectomy
 - Straddle PE
 - IVC
 - DVT
 - High energy devices

Status of Availability of Thromboprophylaxis and Thrombolytic Therapy in RSA

- The public sector has major deficiencies or
- At best erratic provisioning for thromboprophylaxis and thrombotherapy
- Almost universal lack of mechanical devices for thromboprophylaxis
- Limited repertoire of treatment options

Intermittent Pneumatic Compression or Graduated Compression Stockings for Deep Vein Thrombosis Prophylaxis?

A Systematic Review of Direct Clinical Comparisons Rhys J. Morris, PhD,* and John P. Woodcock, DSc⁺

- The difference in DVT outcome only reached statistic significance in 3, and all showed IPC to have the lower DVT rate.
- The crude cumulative DVT rate for all the trials was 5.9% for GCS and 2.8% for IPC.

(Ann Surg 2010;251: 393–396)

Comparative Effectiveness of Combined Pharmacologic and Mechanical Thromboprophylaxis versus Either Method Alone in Major Orthopedic Surgery: A Systematic Review and Metaanalysis

Diana M. Sobieraj, Craig I. Coleman, Vanita Tongbram, Wendy Chen, Jennifer Colby, Soyon Lee, Jeffrey Kluger, Sagar Makanji, Ajibade Ashaye, and C. Michael White

- The risk of deep vein thrombosis (DVT) was significantly decreased in the combination group (relative risk [RR] 0.48 [95% confidence interval (CI) 0.32–0.72]), with moderate strength of evidence
- Conclusions. The risk of DVT was decreased with the use of combination prophylaxis versus pharmacologic prophylaxis alone in patients undergoing total hip replacement or total knee replacement.

(Pharmacotherapy 2013;33(3):275-283)

Stratified Meta-Analysis of Intermittent Pneumatic Compression of the Lower Limbs to Prevent Venous Thromboembolism in Hospitalized Patients

Kwok M. Ho, MPH, PhD, FRCP; Jen Aik Tan, MBBS

 Conclusions—IPC was effective in reducing venous thromboembolism, and combining pharmacological thromboprophylaxis with IPC was more effective than using IPC alone.

(Circulation. 2013;128:1003-1020.)

Management of Post-Thrombotic or Post-Phlebitic Syndrome

- Long term effect of thrombotic obstruction of veins 48%
- Venous valvular incompetence from "thrombotic" obstruction 27%
- Combination thrombotic obstruction and valvular incompetence 54%
 - \rightarrow Venous hypertension
 - \rightarrow Peripheral oedema
 - \rightarrow Hypoxia
 - \rightarrow Tissue death ulceration
 - fibrosis
- Treatment by
 - Exercise
 - Compression stocking
 - Manage ulceration

Management of Pulmonary Embolism

- Haemodynamically stable patient
 - ightarrow Standard anticoagulation therapy
 - → IVC filter if anticoagulation therapy is contra-indicated or recurrent despite anticoagulation
 - le ana dura micellu un stable nationt
- Haemodynamically unstable patient
 - ightarrow Thrombolytic therapy
 - \rightarrow Embolectomy
 - * Surgical
 - * Catheter directed thrombolysis
 - Ultrasound assisted
 - Rheolytic (high pressure saline) embolectomy
 - Suction (aspiration) embolectomy
 - rotation catheter fracture embolectomy
- Prognosis varied depending on haemodynamic status and co-morbidities
- Chronic thromboemobolic pulmonary hypertension rare
- Prognostic score Pulmonary Embolism Severity Index (PESI) available

Patient group	Prevalence of deep vein thrombosis (%)
General medical	10-20
General surgery	15-40
Major gynaecological surgery	15-40
Stroke	20-50
Hip or knee arthroplasty, hip fracture surgery	40-60
Major trauma	40-80
Critical care	10-80

Absolute risk of deep vein thrombosis in hospital inpatients

Cayley WE BMJ 2007

Box 2 | Methods of prophylaxis against DVT in hospital inpatients

- Graduated compression stockings
- Intermittent pneumatic compression
- Aspirin
- Unfractionated heparin
- Low molecular weight heparins (enoxaparin, dalteparin)
- Vitamin K antagonists (warfarin, acenocoumarol, phenindione, and dicoumarol)
- Fondaparinux

Cayley WE BMJ 2007

Risk level	Calf DVT	Proximal DVT	Clinical PE	Fatal PE
Low risk	2%	0.4%	0.2%	<0.01%
Minor surgery in patients aged $<$ 40 y with no additional risk factors				
Moderate risk	10%-20%	2%-4%	1%–2%	0.1%-0.4%
Minor surgery in patients with additional risk factors				
Surgery in patients aged 40–60 y with no additional risk factors				
High risk	20%-40%	4%-8%	2%-4%	0.4%-1.0%
Surgery in patients >60 y or with additional risk factors (eg, prior VTE, cancer)				
Highest risk	40%-80%	10%–20%	4%-10%	0.2%-5%
Surgery in patients with multiple risk factors (age $>$ 40 y, cancer, prior VTE)				
Hip or knee arthroplasty, hip fracture surgery				

TABLE 1. Degree of Thromboembolism Risk in Surgical Patients Without Prophylaxis

Adapted from Geerts WH, Heit JA, Clagett GP, et al. Chest. 2001;119(suppl 1):132S-175S.

Agnelli G Circulation 2004

At-Risk Population	Recommendations	
American College of Chest Physicians ⁴		
Hiahest risk	Low-dose LMWH	
Surgery in patients with multiple risk factors (age >40 y, cancer, prior	• Fondaparinux 2.5 mg/d	
VTE)	 Oral anticoagulants (target INR 2-3) 	
Hip or knee arthroplasty, hip fracture surgery Major trauma, spinal cord injury	IPC or GCS+LDUH or low-dose LMWH	
High risk	LDUH q8 hours	
Surgery in patients >60 y or 40–60 y of age with additional risk factors (prior VTE, cancer, molecular hypercoagulability)	Low-dose LMWH IPC	
Moderate risk	LDUH q12 hours	
Minor surgery in patients with additional risk factors	Low-dose LMWH	
Surgery in patients 40–60 y of age with no additional risk factors	• GCS	
	• IPC	
Low risk	 No specific prophylaxis 	
Minor surgery in patients <40 y of age with no additional risk factors	 Early and "aggressive" mobilization 	
Surgical Care Improvement Project ²¹		
General surgery with moderate to high risk for VTE	• LDUH	
	Low-dose LMWH	
	LDUH or low-dose LMWH+IPC or GCS	
General surgery with high risk for bleeding	GCS	
International Union of Angiology ²²		
High risk	 LDUH 5000 U 2 h before operation, continued q8 h until patient is 	
Major surgery, age >60 y	ambulatory with or without GCS or IPC	
Major surgery, age 40–60 y, and cancer or history of DVT/PE	Low-dose LMWH initiated and dosed according to manufacturers'	
Thrombophilia	recommendations with or without GCS or IPC	
	• Fondaparinux	
Moderate risk	 LDUH 5000 U 2 h before operation, continued q12 h or q8 h until patient is 	
Minor surgery, age >60 y	ambulatory	
Major surgery, age 40-60 y with history of DVT/PE or on estrogen	 Low-dose LMWH Initiated and dosed according to manufacturer's recommendations for medicrate risk patients. 	
minor surgery, age 40-00 y with history of DV1/FE of on estrogen therapy	 IPC+GCS until nation is ambulatory especially in nations at risk for or with 	
unapy	active bleeding	
Low risk	Insufficient data to make firm recommendations, but consider GCS, early	
Major surgery, age <40 v with no additional risk factors	ambulation, adequate hydration.	
Minor surgery, age 40–60 y with no additional risk factors	• LDUH 5000 U	
Patients undergoing laparoscopic surgery, with additional risk factors	Low-dose LMWH IPC+GCS	
National Comprehensive Cancer Network ²³		

Adult inpatients with diagnosis or clinical suspicion of cancer, without relative contraindication to anticoagulation

Adult inpatients with diagnosis or clinical suspicion of cancer, with relative contraindication to anticoagulation present

- Low-dose LMWH
- Fondaparinux 2.5 mg/d
- LDUH 5000 U q8 h
- · With or without IPC
- Mechanical prophylaxis: IPC or GCS

INR indicates international normalized ratio; IPC, intermittent pneumatic compression; GCS, graduated compression stockings; q8 h, every 8 hours; and q12 h, every 12 hours.

Zurawska U Circulation 2007

Villalta scale	CEAP
Symptoms:	Clinical:
Heaviness	0-None
Pain	1–Telangiectasis
Cramps	2-Varicosities
Pruritus	3–Edema
Parathesis	4–Pigmentation,
Signs:	lipodermatosclerosis
Pretibial edema	5–Ĥealed ulceration
Induration	6–Ulcer
Hyperpigmentation	Etiology:
New venous ectasia	Congenital/primary/secondary
Redness	Anatomic distribution:
Pain of calf compression	Superficial, deep, perforator, or
(Ulceration receives a	combination
score of 15)	Pathophysiology:
Each factor is scored: 0	Reflux, obstruction, or
(none) to 3 (severe)	combination
Mild: score 5-9	Severe:
Moderate: score 10-14	$> C_4$
Severe: score >15	•

Table I. Postthrombotic syndrome classification^a

^aAdapted from Kahn et al⁷ and Eklof et al.⁸



Fig 1. Hypothetic basic mechanism is shown of early and later deep venous thrombosis-mediated vein wall injury of the whole vein. *LDS*, Lipodermatosclerosis; *MMP*, matrix metalloproteinase; *PMN*, polymorphonuclear neutrophil; *TF*, tissue factor; *VSU*, venous stasis ulcer.

Henke PK J Vasc Surg 2011

Factor	Fold increase
Unprovoked deep venous thrombosis	~2-3
Active malignancy	2-4
Antiphospholipid syndrome	2-8
Iliofemoral location	~2-3
Increasing age	+/-
Gender (male > female)	~2

Table II. Factors associated with deep venous thrombosis recurrence

Henke PK J Vasc Surg 2011

Symptoms and Clinical signs	None	Mild	Moderate	Severe
Symptoms				
Pain	0 points	1 point	2 points	3 points
Cramps	0 points	1 point	2 points	3 points
Heaviness	0 points	1 point	2 points	3 points
Paresthesia	0 points	1 point	2 points	3 points
Pruritus	0 points	1 point	2 points	3 points
Clinical signs				
Pretibial edema	0 points	1 point	2 points	3 points
Skin induration	0 points	1 point	2 points	3 points
Hyperpigmentation	0 points	1 point	2 points	3 points
Redness	0 points	1 point	2 points	3 points
Venous ectasia	0 points	1 point	2 points	3 points
Pain on calf compression	0 points	1 point	2 points	3 points
Venous ulcer	Absent	Present		

Table 1 Villalta's PTS scale [17]

Points are summed into a total score (range 0–33). PTS is defined by a total score of ≥ 5 or the presence of a venous ulcer. PTS is classified as *mild* if the Villalta score is 5–9, *moderate* if the Villalta score is 10–14, and *severe* if the Villalta score is ≥ 15 or a venous ulcer is present. To use the Villalta score as a continuous measure, it is recommended that patients who meet criteria for severe PTS based solely on the presence of an ulcer (i.e. total Villalta score is <15) be assigned a score of 15 [2].

Kahn SR et al J Throm Haem 2009

PAUSE

SCENARIOS FOR CONTROVERSIES SYMPOSIUM ETHICS SESSION 4TH OCTOBER 2015

<u>Scenario</u>

A 55 yr old self-employed motor mechanic presents with a sudden onset of pain in the LIF. He had been experiencing a change in bowel habit in recent months. He is pyrexial with a tachycardia but has a normal blood pressure on regular antihypertensive medication. He has a tender mass in the LIF. An abdominal ultrasound shows a mass with complex fluid and some gas. A differential diagnosis of a perforated diverticular disease or perforated rectosigmoid cancer was made. The WBC was 13, HB 12, UKE and CPM were within normal limits. 1. What would be the next step?

Possibilities – investigate further with a CT scan

(?Sigmoidoscopy contra-indicated)

CT Scan shows a mass lesion in the rectosigmoid region which has perforated.

2. What would one do next?

Possibilities: Operate now or Give an antibiotic to settle down the infection before exploration.

But does not settle

3. Whether immediate or delayed, what operation should be undertaken?

(Local percutaneous drainage is not an option in cancer patients) \rightarrow Exploratory lap.

4. What preparation should be made for the patient?

Possibilities: Anticoagulation prophylaxis – and how?

a. LMWH or unfractionated heparin availableb. Graduated stockings not available (patients may purchase their own but your patient cannot afford)

c. Intermittent calf pressure pumps not available

5. What next? Use LMWH now or use within 12 hrs post-op and do an exploratory operation?

At operation an inflammatory mass in the left iliac fossa was mobilised with difficulty but resected completely. The cut surface macroscopically appears malignant. Blood loss was about 1 litre. Blood transfusion was started. Patient needed inotropes to maintain BP intra-op.

6. Should a primary anastomosis be done?

Issues:

- (1) Blood loss and circulatory instability
- (2) Perforated carcinoma

7. Should a Hartmann's procedure be performed?

8. Patient taken to ICU post-op. When would LMWH be recommenced.

?Delay recommencement LMWH for 12 hrs

9. On day 2 in ICU the patient's respiration has deteriorated. What could be the issues?

?ARDS - CXR equivocal
?PE - CT angio → PE
Confirm DVT

10. What next?

 \rightarrow ? Medical thrombolysis

Fear of rebleeding after high operative blood loss

 \rightarrow ? Surgical IVC filter

Patient recovers from ICU and is discharged home with a stoma 14 days later

11. What treatment would you offer him now?

- 12. Start Warfarin or Factor X a Inhibitor (but not available)?
- 13. When should we remove the IVC filter?

14. Should we reverse the Hartmann's procedure?

If so when?

15. What are the VTE issues?

16. What preparation for reversal Hartmann's?

Issues: Recurrent thrombosis Phasing out oral anticoagulant Commence parenteral

17. What operation strategy should be adopted?

- Need to shorten operation time
- Mechanical stapling device closure vs hand sew closure.
 (No mechanical staplers in stock until next budget cycle in 4 months)

18. What do we do?

- Delay
- or counsel patient for possible DVT and proceed with op?

19. What treatment post-op?

20. When should the IVC filter be removed?

What are the medicolegal issues

- Undertaking emergency surgery in very high risk pt without optimal thromboprophylaxis
- Nursing pt in ICU postop without adequate thromboprophylaxis
- Elective reversal of Hartmann's without adequate thromboprophylaxis even with pt informed consent (pt has not been back to work to afford own compression stocking)
- The patient wants to sue for VTE episode-who is liable, doctor, the hospital, the provincial health authority